DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

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APR 14 2000

Mikart Inc.
Attention: Cerie McDonald
1750 Chattahoochee Ave.
Atlanta, GA 30318

Docket No. 99P-2150/CP1

Dear Ms. McDonald:

This is in response to your petition filed on July 2, 1999, requesting permission to file Abbreviated New Drug Applications (ANDAs) for the following drug products: Butalbital, Acetaminophen, and Caffeine Tablets and Capsules, 50 mg/750mg/40mg. The listed drug product to which you refer in your petition is Esgic Plus® (Butalbital, Acetaminophen, and Caffeine) Tablets, 50 mg/500 mg/40mg, manufactured by Mikart, Inc.

Your request involves a change in dosage form (i.e., from tablets to capsules) and a change in strength of the acetaminophen component (i.e., from acetaminophen 500 mg to acetaminophen 750 mg) from that of the listed drug product. The changes you request are the type of changes that are authorized under the Act.

We have reviewed your petition under Section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act (Act) and have determined that it is approved. This letter represents the Agency's determination that ANDAs may be submitted for the above-referenced drug products.

In addition, this petition was evaluated with respect to the Regulations Requiring Manufacturers to Assess the Safety and Effectiveness of New Drugs and Biological Products in Pediatric Patients; Final Rule, published in the Federal Register (Pediatric Rule)(63 FR 66632). The agency has determined that your proposed change in dosage form is subject to the Pediatric Rule, but has concluded that investigations are not necessary to demonstrate the safety and effectiveness of your proposed product in the pediatric population, because this specific drug product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients and is not likely to be used in a substantial number of pediatric patients. The listed drug product that you cite as the basis of your petition is labeled for Pediatric Use. Specifically the labeling states; "Safety and effectiveness in pediatric patients below the age of 12 have not been established". However, your proposed drug product cannot be labeled for use in pediatrics because the dose of acetaminophen exceeds the amount that is safe for use in this population. When you submit your application the labeling for Pediatric Use should be revised to state; "Safety and effectiveness in pediatric patients have not been established."

Under Section 505(j)(2)(C)(i) of the Act, the Agency must approve a petition seeking a dosage form and strength which differ from the dosage form and strength of the listed drug product unless it finds that investigations must be conducted to show the safety and effectiveness of the differing dosage form and strength.

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The Agency finds that the change in dosage form and strength for the specific proposed drug products do not pose questions of safety or effectiveness. The Agency concludes, therefore, that investigations are not necessary in this instance. In addition, if shown to meet bioavailability requirements, the proposed drug products can be expected to have the same therapeutic effect as the listed reference drug product.

When you submit your ANDAs, in addition to the revision of the pediatric use section noted above, the proposed labeling should reflect the maximum number of tablets per day that can be administered for your proposed drug products (i.e., 5 tablets). The total daily dose of the acetaminophen component should not exceed the maximum total daily dose for adults of 4000 mg established by the Agency for its safe and effective range. Please refer to the Tentative Final Monograph for Internal Analgesic, Antipyretic, and Antirheumatic Drug Products for Over-the-Counter Human Use (53 FR 46204, November 16, 1988).

The approval of this petition to allow ANDAs to be submitted for the above-referenced drug products does not mean that the Agency has determined that ANDAs will be approved for the drug products. The determination of whether an ANDA will be approved is not made until the ANDA itself is submitted and reviewed by the Agency.

To permit review of your ANDA submissions, you must submit all information required under Sections 505(j)(2)(A) and (B) of the Act. To be approved, the drug product will, among other things, be required to meet current bioavailability requirements under Section 505(j)(2)(A)(iv) of the Act. We suggest that you submit your protocol to the Office of Generic Drugs, Division of Bioequivalence for this drug product prior to the submission of your ANDAs. During the review of your application, the Agency may require the submission of additional information.

The listed drug product to which you refer in your ANDA must be the one upon which you based this petition. In addition, you should refer in your ANDA to the appropriate petition docket number cited above, and include a copy of this letter in the ANDA submission.

A copy of this letter approving your petition will be placed on public display in the Dockets Management Branch, Room 1061, Mail Stop HFA-305, 5630 Fishers Lane, Rockville, MD 20852.

Sincerely yours,

Gary J. Buehler
Acting Director
Office of Generic Drugs
Center for Drug Evaluation and Research